REMARKS

Claims 1-2 and 4-41 are pending, applicants having previously canceled claim 3. Applicants acknowledge with appreciation the Examiner's withdrawal of the claim rejections under 35 U.S.C. §112 and 35 U.S.C. §102. In the Final Office Action now under reply, the claims have been rejected as follows:

(1) claims 1-2, 4-10, 12-31, 34-35, 37-38, and 40-41 are rejected under 35 U.S.C. §103(a) as unpatentable over Kim et al., US 5,455,044 ("Kim") in view of Penners et al., US 6,306,439, ("Penners");

(2) claim 11 is rejected under 35 U.S.C. §103(a) as unpatentable over Kim in view of Penners and further in view of Chen et al., *Proc. Nat. Acad. Sci.*, 2002, 99(13), 9031-9036 ("Chen");

(3) claim 32 is rejected under 35 U.S.C. §103(a) as unpatentable over Kim in view of Penners, further in view of Chen, and further in view of Hatcher et al., *Soc. For Neurosciences*, 19th Annual Meeting, Abs. #236.4, Oct. 23-28, 1999 ("Hatcher"); and

(4) claims 36 and 39 are rejected under 35 U.S.C. §103(a) as unpatentable over Kim in view of Penners, and further in view of Russell et al. *Bone Marrow Transplantation*, 1999, 24, 1177-1183 ("Russell").

Applicants note that the status of claim 33 is not mentioned in the Detailed Action, but is included with the rejected claims on the Office Action Summary.

The rejections are overcome in part by the amendments made herein, and are otherwise traversed for at least the reasons set forth below.

Claim Amendments

Claim 1 has been amended to recite that the biocompatible composition is suitable for administration to the cerebrospinal fluid of a subject. Support for this amendment is provided, for example, in the original specification at page 3, lines 30-31. Accordingly, no new matter is added by these amendments.

First rejection under 35 U.S.C. §103(a)

Claims 1-2, 4-10, 12-31, 34-35, 37-38, and 40-41 are rejected under 35 U.S.C. §103(a) as unpatentable over Kim in view of Penners. The Examiner cites the reasons set forth in the Office Action dated June 2, 2006 ("the June 2006 Action"). This rejection is traversed.

The compositions and methods described by the pending claims are not obvious extensions of the technologies described by Kim, Penners, or any purported combination of Kim and Penners. The skilled artisan would have no reason to combine the teachings of Kim with those of Penners, but would, in fact, have reason not to combine such teachings. These conclusions are set forth and discussed in Applicant's response dated December 4, 2006 ("the December 2006 response"). Further explanation of applicant's reasoning, as well as additional evidence and arguments, are set forth below.

In the June 2006 Action, it is stated that Kim lacks the teachings of a specific buoyancy agent, and that Penners provides such teachings. It is also stated that Penners teaches that the gas-forming substances in his composition evolve non-toxic gases upon contact with water. The June 2006 Action concludes that it would have been obvious to a person of ordinary skill at the time of the instant invention to combine the teachings of Kim and Penners.

As pointed out in the December 2006 response, and as supported by the declaration under 37 C.F.R. §1.132 by Dr. Tim Maher (submitted herewith as Exhibit A), combining the teachings of Kim with those of Penners would not have been obvious to the skilled artisan. In fact, the skilled artisan would have been *highly discouraged* from making such a combination. Kim relates to compositions suitable for delivery to the central nervous system (CNS) of a patient, while Penners relates to compositions suitable for delivery to the gastrointestinal (GI) tract of a patient. Because of the physiological differences between the CNS and the GI tract, compositions suitable for administration to one are not necessarily suitable for administration to the other. The compositions described by Penners and cited by the Examiner involve the degradation of hydrogen carbonates, a reaction that produces carbon dioxide and hydroxide ion. The December 2006 response and the declaration of Dr. Maher establish that the skilled artisan would have been discouraged from combining the teachings of the cited references at least because the hydroxide ion produced by the degradation reaction described in Penners has the potential to cause serious adverse side effects when applied to compositions intended to be administered to the CNS. In essence, the highly sensitive nature of the CNS preclude the use of a

many of compositions that are designed for administration to the GI tract. There is therefore a high probability that the skilled artisan would have been motivated to *avoid* combining the teachings of Kim with the teachings of Penners, as evidenced by Dr. Maher's Declaration and the arguments set forth in the December 2006 response.

In addition, Kim does not, in fact, teach that the specific gravity or buoyancy of polymer particles within the cerebrospinal fluid (CSF) may be varied. Kim teaches dispersion systems that contain a dispersed phase (e.g., beads, micelles, microspheres, etc.) and a water phase. Kim states that "the density of the dispersion system can be modified by altering the specific gravity to make the dispersion hyperbaric or hypobaric." By this statement, Kim is teaching modification of the density of the dispersion as a whole. Such modification is practically accomplished by altering the density of the *water phase* (as opposed to the density of the particles of the *dispersed phase*). This distinction is supported by the examples of additives cited by Kim as useful for modifying the density of the dispersion material: iohexol, iodixanol, metrizamide, sucrose, trehalose, glucose, or other biocompatible molecules with high specific gravity. All of these additives are highly water soluble, indicating that Kim is describing modification of the density of the water phase.

The distinction between modifying the density of the water phase, as taught by Kim, and modifying the density of the dispersed phase, as taught by the present application, is of vital importance. The density of the dispersed phase is modified in the present application in order to adjust the buoyancy of the polymer particles *within the CSF*. In the systems taught by Kim, however, the water phase of the dispersion system is quickly absorbed into the surrounding liquid (i.e., the water phase is simply a carrier for the particles) upon administration to a patient's CSF. Therefore, adjusting the density of the water phase, as described by Kim, may affect the buoyancy of the particles within the *water phase*, but would have little or no effect on the buoyancy of the particles *within the CSF*. In other words, Kim provides a method for adjusting the density of the dispersion systems during their preparation (i.e., in vitro) rather than during their administration (i.e., in vivo). Kim neither teaches nor suggests a composition that is controllably buoyant *within the cerebrospinal fluid*, as recited in the instant claim 1.

For at least the foregoing reasons, the combination of Penners and Kim do not render obvious claims 1-2, 4-10, 12-31, 34-35, 37-38, and 40-41, and applicants respectfully request withdrawal of the rejection.

Second rejection under 35 U.S.C. §103(a)

Claim 11 stands rejected under 35 U.S.C. §103(a) as unpatentable over Kim in view of Penners and further in view of Chen. The Examiner states that both Kim and Penners lack the teaching of a biocompatible composition wherein the therapeutic agent is selected from the group of inosine, citicholine, superoxide dismutase, and dextrophan, and that this deficiency is cured by the teachings of Chen (Action of June 2, 2006, page 13). This rejection is traversed.

The merits of the combination of Kim and Penners are discussed above. In summary, one of ordinary skill in the art would find no motivation to combine the teachings of Penners with Kim, at least for the reason that the compositions of Penners would generate byproducts that are potentially toxic to the CNS and are therefore unsuitable for administration to the CSF.

Regardless of the therapeutic agents that are employed, the teachings of Chen do not provide the motivation that would be needed to combine the teachings of Kim with the teachings of Penners. Chen is directed to the effects of inosine on rats suffering from certain types of strokes. Chen does not address biocompatible compositions suitable for administration to the cerebrospinal fluid of a subject comprising a plurality of polymer particles, as claimed. Therefore, Chen does not address the deficiencies of either Kim or Penners, or the combination of Kim with Penners as described above, with respect to claim 1 (and claims dependent thereon, including claim 11). Any combination of Chen with Kim or Penners (or both) fails to teach the claimed invention; accordingly, applicants respectfully request withdrawal of the rejection.

Third rejection under 35 U.S.C. §103(a)

Claim 32 stands rejected under 35 U.S.C. §103(a) as unpatentable over Kim in view of Penners, further in view of Chen, and further in view of Hatcher. The Examiner contends that Kim, Penners, and Chen lack the teaching of a composition comprising both inosine and citicholine as therapeutic agents, and that this deficiency is cured by the teachings of Hatcher (Action of June 2, 2006, page 14). This rejection is traversed.

The merits of the combination of Kim, Penners, and Chen are discussed above. In summary, one of ordinary skill in the art would find no motivation to combine the teachings of Penners with Kim, at least for the reason that the compositions of Penners would generate byproducts that are potentially toxic to the CNS and are therefore unsuitable for administration to

the CSF. Furthermore, Chen does not provide the motivation that would be required to combine the teachings of Kim with those of Penners.

Regardless of the therapeutic agents that are employed, the teachings of Hatcher do not provide the motivation that would be needed to combine the teachings of Kim with those of Penners and with those of Chen. Hatcher is directed to the neuroprotective effect of CDP-choline in hippocampal CA_1 region after transient ischemia of gerbils (see Abstract). Hatcher does not address biocompatible compositions suitable for administration to the cerebrospinal fluid of a subject comprising a plurality of polymer particles, as claimed. Therefore, Hatcher does not address the deficiencies of Kim, Penners, Chen, or any combination thereof, as described above, with respect to claim 12 (and claims dependent thereon, including claim 32). Accordingly, applicants respectfully request withdrawal of the rejection.

Fourth rejection under 35 U.S.C. §103(a)

Claims 36 and 39 stand rejected under 35 U.S.C. §103(a) as unpatentable over Kim in view of Penners, and further in view of Russell. The Examiner states that Kim and Penners lack the teaching of living cells as therapeutic agents, and that this deficiency is cured by the teachings of Russell (Action at page 16). This rejection is traversed.

The merits of the combination of Kim and Penners are discussed above. In summary, one of ordinary skill in the art would find no motivation to combine the teachings of Penners with Kim, at least for the reason that the compositions of Penners would generate byproducts that are potentially toxic to the CNS and are therefore unsuitable for administration to the CSF.

Regardless of the therapeutic agents that are employed, the teachings of Russell do not provide the motivation that would be needed to combine the teachings of Kim with the teachings of Penners. Russell is directed to the treatment of leukemia using living cells as therapeutic agents. Russell does not address biocompatible compositions suitable for administration to the cerebrospinal fluid of a subject comprising a plurality of polymer particles as claimed. Therefore, Russell does not address the deficiencies of either Kim or Penners, or the combination of Kim with Penners as described above, with respect to claims 1 or 22 (and claims dependent thereon, including claims 36 and 39). Any combination of Russell with Kim or Penners (or both) fails to teach the claimed invention; accordingly, applicants respectfully request withdrawal of the rejection.

CONCLUSION

Applicants submit that the claims of the application are in condition for allowance. Applicants respectfully request withdrawal of the rejections, and prompt issuance of a notice of allowance. If the Examiner has any questions concerning this communication, or would like to discuss the application, the art, or other pertinent matters, a telephone call to the undersigned would be welcomed.

Respectfully submitted,

By: 

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